REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-31 have been cancelled without prejudice or disclaimer thereto.

Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

New claims 32-39 have been added.

Support for new claims 32 and 34-39 can be found in original claims 1 and 3 (Group II) and in the disclosure, for example, at page 7, lines 21-37, page 23, lines 1-28, page 26, last line to page 27, line 28 and page 35, line 14 to page 36, line 30.

New claim 33 corresponds to original claim 2.

No new matter has been added.

Claims 32-39 are pending upon entry of this amendment.

II. RESPONSE TO RESTRICTION

On page 3 of the Restriction Requirement, it was indicated that the claimed invention does not distinguish over Luster et al., U.S. 5,824,299.

For the sole purpose of expediting prosecution and not to acquiesce to the rejection, claims 1-31 have been canceled without prejudice or disclaimer thereto. New claims 32-39 have been added. The new claims correspond to the method in Group II (claim 3).

Applicants hereby elect the invention set forth in new claims 32-39. Please examine the new claims as the elected invention as they correspond to Group II (claim 3).

Applicants further traverse the Office's position that the claimed invention does not distinguish over Luster et al., U.S. 5,824,299.

Luster et al., U.S. 5,824,299 disclose a pharmaceutical composition or drug comprising an effective amount of IP-10 protein that expressly has the activity of activating immunocyte (T cell) migration. In other words, Luster et al. only disclose that IP-10 promotes the migration of immune cells, particularly T cells.

In contrast, the present invention is based on the novel finding that IP-10 activates embryo implantation in the mother. As such, the Applicants have succeeded in finding that IP-10 promotes embryo implantation to a mother. The claims set forth in the present application are based on this novel finding.

Trophoblast cells are completely different from immune cells and blood cells. Trophoblast cells enclose an embryo, and attach to the mother. Thus, the trophoblast is a cell population associated with placentation. Since IP-10 is capable of controlling migration of trophoblasts, it is clear that the implantation of embryo can be promoted by use of IP-10.

Luster et al. does not disclose or suggest the above-noted aspects of the invention.

At present, it is reported that only about 50% of fertilized eggs are successfully implanted, and pregnancy depends on this percent implantation. The Fertilization and Implantation Group, Japan Society of Obstetrics and Gynecology (JSOG) has reported that fertilization is not the start of a life, but the life is initiated by embryo implantation/placentation.

By using the present invention, it will be now possible to increase embryo implantation rates, resulting in 2-fold increase in pregnancy.

Thus, it is respectfully submitted that the claimed invention is neither disclosed nor suggested by Luster et al., U.S. 5,824,299.

In addition, Applicants wish to note the following unique new findings on which the present invention is based.

For chemokine IP-10, recombinant IP-10 proteins have the following actions at a dose of 20ng/ml under cell culture conditions:

Action 1 - Chemokine IP-10 stimulates a 1.5 to 2-fold increase in the migration of trophoblast cells. Please see Attachment 2 (Nagaoka et al., J. Biol Chem., Vol. 278(31), pp. 29048-29056 (2003)).

Action 2 - Chemokine IP-10 induces about a 20-fold increase of specific chemokine receptor CXCR3 (IP-10 receptor) expression in trophoblast cells. See Nagaoka et al.

Action 3 - Chemokine IP-10 elevates trophoblast cell adhesion to endometrium by 2- to 3-fold. See Nagaoka et al. and Attachment 3 (Imakawa et al., Molecular Reproduction and Development, vol. 73, pp. 850-858 (2006)).

Action 4 – Chemokine IP-10 induces a 2- to 3-fold increase in the expression of integrins (integrin α_5, α_v and β_3) in trophoblast cells. This elevated integrin expression causes an increase in the adhesion of trophoblast cells to uterine epithelial cells (See Nagaoka et al.). It is believed that this adhesion takes place depending on the extracellular matrix (fibronectin) on the uterine epithelial cell (please note fibronectin is a substrate for the fibronectin receptor, integrin). Actually, when conceptus trophoblast cells were incubated with fibronectin, adhesiveness on day 17 (implantation initiation) and day 20 was elevated by about 5-fold and about 7-fold, respectively, as compared with that on day 14 (Imakawa et al.).

Action 5 - IP-10 is involved with the migration of NK cells in the presence of the pregnancy hormone (progesterone).

Kindly note that, in Luster et al., IP-10 is T cell-specific, while in uterus it does not affect T cells but is involved in the migration of NK cells.

Further, it facilitates the expression of interleukin 10 (IL-10) (essential for establishment of pregnancy) from NK cells. See Attachment 4: (Nagaoka et al., AJRI, Vol. 53: pp. 54-64 (2005)) and Imakawa et al.

For mechanisms associated with IP-10, please also refer to the 4 slides in Attachment 1.

It is respectfully submitted that the cited prior art fails to disclose or suggest the above-noted unique aspects of the present invention.

Favorable action on the merits is now requested.

Respectfully submitted,

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ATTACHMENTS

1. Four slides;
2. Nagaoka et al., J. Biol Chem., Vol. 278(31), pp. 29048-29056 (2003);
3. Imakawa et al., Molecular Reproduction and Development, vol. 73, pp. 850-858 (2006); and
4. Nagaoka et al., AJRI, Vol. 53: pp. 54-64 (2005).